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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SMITH, CAROLYN L	

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1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,937	MENDRICK ET AL.	
	Examiner	Art Unit	
	Carolyn Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *8,10,11,22-47,50-52,55 and 57-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,12-21,48,49,53,54,56 and 61-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02272007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I (claims 1-7, 9, 12-21, 48-49, 53-56, and 61-66) and species A (SEQ ID NO: 1923, sorbitol dehydrogenase), B (arrhythmias), C (cyclophosphamide), D (microarray assays), filed 10/1//09, is acknowledged. Claim 55 is withdrawn due to being drawn to a non-elected specie. Claims 8, 10-11, 22-47, 50-52, and 57-60 are withdrawn due to being drawn to non-elected Groups.

The information disclosure statement filed 2/27/07 fails to comply with the provisions of 37 CFR 1.97, 1.98, and MPEP § 609, because references 98, 301, and 316 lack a publication date and/or the place of publication. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609, ¶ C(1). All of the remaining references in the IDS, filed 2/27/07, have been considered by the Examiner.

Claims herein under examination are 1-7, 9, 12-21, 48-49, 53-54, 56, and 61-66.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, such as in paragraphs 0006 and 00140. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claims are not patentably distinct from the reference claims because the examined claims are either anticipated by, or would have been obvious over the reference claims. *See, e.g., In re Berg,* 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Claims 1-7, 9, 12-21, 48-49, 53-54, 56, and 61-66 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 7,447,594.

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 1-10 and related passages in the specification of patent '594 encompass all elements of instant claims 1-7, 12-20, 48-49, 53-54, 56, and 61-65.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claim 1 of patent '594 recites a method of determining whether a test compound is a cardiotoxin comprising steps of preparing an expression profile of at least ten genes from tissue or cell sample exposed to a test compound and comparing the profile to a model comprising data of Tables 5A-5LL.

The examiner assumes that some genes in Tables 5A-5LL of both application and patent overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the obviousness-type double patenting rejection.

Thus, claims 1-10 of U.S. Patent No. 7,447,594 make obvious instant claims 1-7, 9, 12-21, 48-49, 53-54, 56, and 61-66.

Claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 7,415,358.

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 1-10 and related passages in the specification of patent '358 encompass all elements of instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claim 1 of patent '358 recites a method of determining whether a test compound is a renal toxin comprising steps of preparing an expression profile of at least ten genes from tissue or cell sample exposed to a test compound and comparing the profile to a model comprising data of Tables 5-5CC.

The examiner assumes that some genes in Tables 5A-5LL and Tables 5-5CC overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the obviousness-type double patenting rejection.

Thus, claims 1-10 of U.S. Patent No. 7,415,358 make obvious instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 7,426,441.

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 1-14 and related passages in the specification of patent '441 encompass all elements of instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claim 1 of patent '441 recites a method of determining whether a test compound is a renal toxin comprising steps of preparing an expression profile of at least ten genes from tissue or cell sample exposed to a test compound and comparing the profile to a model comprising data of Tables 5-5CC.

The examiner assumes that some genes in Tables 5A-5LL and Tables 5-5CC overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the obviousness-type double patenting rejection.

Thus, claims 1-14 of U.S. Patent No. 7,426,441 make obvious instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 7,590,493.

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 1-10 and related passages in the specification of patent '493 encompass all elements of instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claim 1 of patent '493 recites a method of determining whether a test compound is a hepatotoxin comprising steps of preparing an expression profile of at least ten genes from tissue or cell sample exposed to a test compound and comparing the profile to a model comprising data of Tables 3-3DD.

The examiner assumes that some genes in Tables 5A-5LL and Tables 3-3DD overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-

overlapping, sets of genes, or to file a terminal disclaimer to overcome the obviousness-type double patenting rejection.

Thus, claims 1-10 of U.S. Patent No. 7,590,493 make obvious instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 7,469,185.

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 1-10 and related passages in the specification of patent '185 encompass all elements of instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claim 1 of patent '185 recites a method of determining whether a test compound is a liver toxin comprising steps of preparing an expression profile of at least ten genes from tissue or cell sample exposed to a test compound and comparing the profile to a model comprising data of Tables 5A-5XX.

The examiner assumes that some genes in Tables 5A-5LL and Tables 5A-5XX overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are

invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the obviousness-type double patenting rejection.

Thus, claims 1-10 of U.S. Patent No. 7,469,185 make obvious instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Claims 1, 10, 12, 14, 16-23, 27-28, 44, 46, and 67-68 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 70-79 of copending Application 12/064933 ("App. '933").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 1, 10, 12, 14, 16-23, 27-28, 44, 46, and 67-68 and related passages in the specification of App. '933 encompass all elements of instant claims 1-7, 9, 12-21, 48-49, 53-54, 56, and 61-66.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claims 1, 10, 12, 14, 16-23, 27-28, 44, 46, and 67-68 of App. '933 recite a method of predicting toxicity of a compound comprising steps of preparing/detecting an expression profile of liver tissue or cell sample and comparing the profile to a database comprising data of Tables 1, 2, or 4.

The examiner assumes that some genes in Tables 5A-5LL and Tables 1, 2, or 4 overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the provisional obviousness-type double patenting rejection.

Thus, claims 1, 10, 12, 14, 16-23, 27-28, 44, 46, and 67-68 of App. '933 makes obvious instant claims 1-7, 9, 12-21, 48-49, 53-54, 56, and 61-66.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 70-79 of copending Application 10/501933 ("App. '933").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 70-79 and related passages in the specification of App. '933 encompass all elements of instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claims 70-79 of App. '933 recite a method of predicting toxicity of a compound comprising steps of preparing/detecting an expression profile of liver tissue or cell sample and comparing the profile to a database comprising data of Tables 5A-5WWW.

The examiner assumes that some genes in Tables 5A-5LL and Tables 5A-5WWW overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the provisional obviousness-type double patenting rejection.

Thus, claims 70-79 of App. '933 makes obvious instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-7, 9, 12-21, 48-49, 53-54, 56, and 61-66 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of copending Application 11/600759 ("App. '759").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 1-26 and related passages in the specification of App. '759 encompass all elements of instant claims 1-7, 9, 12-21, 48-49, 53-54, 56, and 61-66.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample

exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claims 1 and 6 of App. '759 recite a method of predicting for the cardiotoxicity of a test compound comprising steps of preparing/detecting a gene expression profile from a tissue or cell sample exposed to a test compound and comparing gene expression profile to data from a database/control, wherein the data are selected from Tables 1-5I.

The examiner assumes that some genes in Tables 1-5I and Tables 5A-5LL overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the provisional obviousness-type double patenting rejection.

Thus, claims 1-26 of App. '759 makes obvious instant claims 1-7, 9, 12-21, 48-49, 53-54, 56, and 61-66.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11, 13, 16-29, 56, and 57 of copending Application 10/515325 ("App. '325").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 1-11, 13, 16-29, 56, and 57 and related passages in the specification

of App. '325 encompass all elements of instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claims 1-11, 13, 16-29, 56, and 57 of App. '325 recite a method of predicting toxicity of a compound comprising steps of preparing/detecting an expression profile of kidney tissue or cell sample and comparing the profile to a database comprising data of Tables 1-5N.

The examiner assumes that some genes in Tables 5A-5LL and Tables 1-5N overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the provisional obviousness-type double patenting rejection.

Thus, claims 1-11, 13, 16-29, 56, and 57 of App. '325 makes obvious instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 and 13-31 of copending Application 10/515373 ("App. '373").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 1-10 and 13-31 and related passages in the specification of App. '373 encompass all elements of instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claims 1-10 and 13-31 of App. '373 recite a method of predicting toxicity of a compound comprising steps of preparing/detecting an expression profile of tissue or cell sample and comparing the profile to a database comprising data of Tables 5A-5MMMMM.

The examiner assumes that some genes in Tables 5A-5LL and Tables 5A-5MMMMM overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the provisional obviousness-type double patenting rejection.

Thus, claims 1-10 and 13-31 of App. '373 makes obvious instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of copending Application 11/642647 ("App. '647").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 1-40 and related passages in the specification of App. '647 encompass all elements of instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claims 1-40 of App. '647 recite a method of predicting toxicity of a compound comprising steps of preparing/detecting an expression profile of tissue or cell sample and comparing the profile to a database comprising data of Tables 5-5L.

The examiner assumes that some genes in Tables 5A-5LL and Tables 5-5L overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the provisional obviousness-type double patenting rejection.

Thus, claims 1-40 of App. '647 makes obvious instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 60-69 of copending Application 12/256225 ("App. '225").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 60-69 and related passages in the specification of App. '225 encompass all elements of instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claims 60-69 of App. '225 recite a method of predicting toxicity of a compound comprising steps of preparing/detecting an expression profile of tissue or cell sample and comparing the profile to a database comprising data of Tables 1 and 3-3DD.

The examiner assumes that some genes in Tables 5A-5LL and Tables 1 and 3-3DD overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-

overlapping, sets of genes, or to file a terminal disclaimer to overcome the provisional obviousness-type double patenting rejection.

Thus, claims 60-69 of App. '225 makes obvious instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2, 5-6, and 10-11 of copending Application 12/434096 ("App. '096").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 1-2, 5-6, and 10-11 and related passages in the specification of App. '096 encompass all elements of instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claims 1-2, 5-6, and 10-11 of App. '096 recite a method of predicting toxicity of a compound comprising steps of preparing/detecting an expression profile of tissue or cell sample and comparing the profile to a database comprising data of Tables 2 and 5.

The examiner assumes that some genes in Tables 5A-5LL and Tables 2 and 5 overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is

noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the provisional obviousness-type double patenting rejection.

Thus, claims 1-2, 5-6, and 10-11 of App. '096 makes obvious instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 55-92 of copending Application 11/790979 ("App. '979").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 55-92 and related passages in the specification of App. '979 encompass all elements of instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claims 55-92 of App. '979 recite a method of predicting toxicity of a compound comprising steps of preparing/detecting an expression profile of tissue or cell sample and comparing the profile to a database comprising data of Tables 3A-3S.

The examiner assumes that some genes in Tables 5A-5LL and Tables 3A-3S overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the provisional obviousness-type double patenting rejection.

Thus, claims 55-92 of App. '979 makes obvious instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6, 11-17, and 19-20 of copending Application 12/043666 ("App. '666").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 55-92 and related passages in the specification of App. '666 encompass all elements of instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

Instant claims 1 and 7 recite a method of predicting for the at least one toxic effect of a compound comprising steps of obtaining a gene expression profile from a tissue or cell sample exposed to a compound and comparing gene expression profile to data from a database/control or detecting expression gene expression level, wherein the data are selected from Tables 5A-5LL.

Claims 6, 11-17, and 19-20 of App. '666 recite a method of predicting toxicity of a compound comprising steps of detecting an expression profile of tissue or cell sample wherein differential expression of genes in Tables 5A-5XX indicates a toxic effect.

The examiner assumes that some genes in Tables 5A-5LL and Tables 5A-5XX overlap because both databases comprise genes expressed in tissue and are indicative of toxicity. It is noted that the retrieval of data from the tables is not a trivial task. Therefore, applicants are invited to present evidence to the contrary, *e.g.,* that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the provisional obviousness-type double patenting rejection.

Thus, claims 6, 11-17, and 19-20 of App. '666 makes obvious instant claims 1-5, 7, 12-20, 48-49, 53-54, 56, and 61-65.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7, 9, 12-21, 48-49, 53-54, 56, and 61-66 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-7, 9, 12-21, 48-49, 53-54, 56, and 61-66 are drawn to a process. A process is statutory subject matter under 35 U.S.C. 101 if: (1) it is tied to a particular machine or apparatus

or (2) it transforms an article to a different state or thing (In re Bilski, 88 USPQ2d 1385 Fed. Cir. 2008).

The claimed subject matter is not limited to a particular apparatus or machine. To qualify as a statutory process, the claims should require use of a machine within the steps of the claimed subject matter or require transformation of an article to a different state or thing. Insignificant extra-solution activity in the claimed subject matter will not be considered sufficient to convert a process that otherwise recites only mental steps into statutory subject matter (In re Grams 12 USPQ2d 1824 Fed. Cir. 1989). Preamble limitations that require the claimed process to comprise machine implemented steps will not be considered sufficient to convert a process that otherwise recites only mental steps into statutory subject matter. It is noted that the instant claim 1 recites "obtaining a gene expression profile"; however, this step is not a transformation of an article to a different state or thing. It is further noted that claims 1-7, 9, 12-21, 48-49, 53-54, 56, and 61-66 do not explicitly require that the steps of the claimed method are performed on a machine. Applicant is cautioned against introduction of new matter in an amendment.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentations is "undue." These factors include, but are not limited to:

a) The breadth of the claims;
b) The nature of the invention;
c) The state of the prior art;
d) The level of one of ordinary skill;
e) The level of predictability in the art;
f) The amount of direction provided by the inventor;
g) The existing of working examples; and
h) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. 858 F.2d at 740. While all of these factors are considered, sufficient amount for a prima facie case are discussed below.

LACK OF ENABLEMENT

Claims 1-7, 9, 12-21, 48-49, 53-54, 56, and 61-66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-7, 9, 12-21, 48-49, 53-54, 56, and 61-66 are not enabled because neither the prior art nor the instant specification teach how to predict toxicity by comparing gene expression to a database, wherein not all genes in Tables 5A-5LL are implicated in toxicity; how to select

genes which are expressed in tissue or cell samples from the tables; and how to compare experimental expression levels and statistical values from the database.

a) The claims are broad because they are drawn to a method for predicting general toxicity (i.e. claim 1) or cardiotoxicity (i.e. claim 7) comprising steps of obtaining a gene expression profile of a tissue or cell sample exposed to a test compound and comparing the expression profile to a database comprising data of Tables 5A-5LL, or merely detecting gene expression levels, thereby predicting cardiotoxicity. The instant specification does not provide specific guidance to practice the invention because it does not disclose how to predict general toxicity or cardiotoxicity for the following reasons:

1) The specification discloses that Table 1 provides the GenBank Accession numbers, Identifier, and SEQ ID NOs. for genes of Tables 5A-5LL. However, not all genes in Table 1 are known to be implicated in toxicity. Tables 1-5 comprise data not only from heart, but also from other tissues/organs, and not all genes are expressed in a particular tissue or cell sample. For example, some of the sequences are isolated from brain, kidney, and testes. Thus, the specification does not provide guidance how to predict toxicity by comparing gene expression to a database or merely detecting gene expression levels, wherein not all genes in Tables 1-5 are expressed in a particular tissue or cell sample, or alternatively may be expressed in multiple tissues. The specification also does not teach how to select genes which *are* expressed in a particular tissue or cell sample from the tables. One skilled in the art would not automatically conclude that a difference among the gene expression profile and data in a database is a prediction in general toxicity or cardiotoxicity. This difference may be due to the fact that the samples are completely unrelated, for example.

2) The specification does not disclose whether the comparison in Tables 1-5 is performed between expression levels in heart OR liver, kidney, brain, *etc.*

3) The instant method recites comparison of expression levels to a database comprising general data or information. The specification does not provide guidance for how to extract expression levels from Tables 1-5 because the tables only disclose statistical values (LDA score, Tox Mean, Tox SD, Non-Tox Mean, Non-Tox SD) obtained, presumably, by further processing expression data; Tables 1-5 do not disclose expression levels. The specification also does not disclose further steps necessary for the comparison of experimental expression levels and statistical values from the database.

4) The specification discloses that Table 1 provides the GenBank Accession numbers, SEQ ID NOs:, and GLGC ID No. for "genes" of Tables 1-5. Table 1 is over 100 pages long. Tables 5A-5LL are over 140 pages long. Tables 5-5LL only comprise GLGC ID Nos. Table 1 comprises GLGC ID Nos. and SEQ ID NOs, both in random order. The specification does not provide guidance how to correlate data of Tables 5A-5LL(*e.g.*, GLGC ID Nos.) to the data of Table 1 (SEQ ID NO, GenBank Acc. No., *etc.*) and to what the data from Tables 5A-5LL correspond. In fact, the examiner was not able to locate the random SEQ ID NO: and GLGC ID NO: in Table 1 and Tables 5A-5LL, despite spending a significant amount of time attempting to do so. Even if one could correlate the data, one would not know which GLGC ID Nos. correspond to expression profile data. Thus, one would not know how to compare the data.

b) The invention is drawn to a method for predicting toxicity.

c) and e) Prior art analysis shows that studying relationships between different genes and compounds requires a correlational database comprising a plurality of standard gene expression

profiles under a plurality of conditions. *See* O'Reilly, WO 02/31704. O'Reilly discloses a database containing expression profiles for a plurality of known genes, wherein profiles are annotated (p. 6-7). The annotations include, for example, information about genes, organisms, tissues, and pathways (pages 6-7). O'Reilly further discloses a database comprising experimental "drug signature" profiles, *i.e.*, expression levels of known genes in known cells in response to a treatment with known compounds and corresponding known biological activities. O'Reilly also discloses comparing expression profiles of known and unknown compounds (claims 1-8). Farr, US 5,811,231, discloses a method of identifying and characterizing the cellular effect of a potential toxin on an animal cell by determining an expression level of known genes in known cells (*e.g.*, liver) treated with known compounds and comparing those data to gene expression of the selected genes treated with an experimental compound in specific cells (example 2, col. 24-25; col. 28, lines 28-35; claims 17-34). The instant specification does not disclose a database comprising genes that are known to be expressed in a particular tissue or cell sample and corresponding expression levels. Further, Friend, US 6,203,987, discloses a method of detecting biological response patterns in response to a drug treatment (col. 6, lines 62-67). Friend discloses acquiring expression data generated with known and unknown compounds, using statistical methods for characterizing cellular responses, and examining similarity of known and unknown responses (col. 9, lines 34-62; col. 14 line 55 through col. 18, line 44). Friend discloses using statistical methods for characterizing both, known and unknown profiles, and comparing statistically evaluated data (col. 10, line 46 through col. 14, line 3; claims 1-3, 10-11). The instant specification does not disclose comparing statistical values of known and unknown responses.

f) The specification does not provide guidance how to predict at least one toxic effect by comparing gene expression levels, *per se*, which are not necessarily involved in at least one toxic effect as the compound the sample is exposed to may lack a toxic effect, to a database comprising statistical data.

g) The specification provides a working example for acquiring expression data from using a microarray technology (Example). However, the specification does not disclose further comparison of the expression levels to a database, *i.e.*, how to pick data from a database, how to process the acquired expression data, and how to compare expression data to a database of statistical values.

h) In order to practice the claimed invention, one skilled in the art must guess which genes are involved in toxicity and must randomly select data from a database. One also must guess what parameters to use for the comparison of expression levels to the claimed database of statistically derived numbers. One skilled in the art would have to guess whether, and what sort of statistical manipulations of the measured expression values are required. The skilled practitioner would further have to guess what the "comparison" represents; *i.e.*, it is unknown which sequences in the claimed tables are upregulated or downregulated and/or how any change in expression is actually related to toxicity. This constitutes undue experimentation.

Due to undue experimentation required, lack of guidance directed to verifying such expression functioning as valid predictors, the lack of working examples addressing the same, the unpredictability of knowing if the expression profile is a potentially valid predictor for toxic effects of compounds, and the breath of the claims; this invention is rejected due to the lack of enablement for one skilled in the art to be able to make and use the invention.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 9, 12-21, 48-49, 53-54, 56, and 61-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of claim 1 recites "predicting at least one toxic effect" whereas the body of the claim recites obtaining and comparing a gene expression profile, but not predicting at least one toxic effect. Therefore, it is not clear if the preamble is intended to limit the method and what relationship is intended between the preamble and method steps. A similar issue is present in claims 7, 9, and 61. Clarification of this issue is requested. Claims 2-6, 12-21, 48-49, 53-54, 56, and 62-66 are also rejected due to their dependency from claims 1, 7, 9, and 61.

Claims 7 (line 2) and 9 (line 2) recite the limitation "the level". There is insufficient antecedent basis for this limitation in the claims as there is no previous mention of a level. Clarification of this issue is requested. Claims 12-21, 48-49, 53-54, and 56 are also rejected due to their dependency from claims 7 and 9.

Claim 9 (line 1) recite the limitation "the cardiotoxicity". There is insufficient antecedent basis for this limitation in the claim as there is no previous mention of cardiotoxicity. Clarification of this issue is requested. Claim 21 is also rejected due to its dependency from claim 9.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran, can be reached on (571) 272-0720.

December 8, 2009

/Carolyn Smith/
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